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FORMULATION AND IN – VITRO EVALUATION OF FLOATING HYDROGEL BEADS OF NIMODIPINE

Ch. Madhavi[1*], Y. Sreelatha[2], V. Jhansi Laxmi [3], Nafees Fatima [4], Dr.N. Sandeepthi[5]

[1] Associate Professor, Department of Pharmaceutics, Sree Dattha Institute of Pharmacy, Ibrahimpatnam, Telangana.,

[2] Assistant Professor, Department of Pharmaceutics, Sree Dattha Institute of Pharmacy, Ibrahimpatnam, Telangana.,

[3] Assistant Professor, Department of Pharmaceutics, Sree Dattha Institute of pharmacy, Ibrahimpatnam, Telangana.,

[4] Assistant Professor, Department of Pharmaceutics, Arya College of Pharmacy, Sanga Reddy, Telangana.,

[5]Associate Professor, Department of Pharmaceutics, Vignan Institute of Pharmaceutical Sciences, Deshmukhi Village, Yadadri Bhuvanagiri Dist.

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Abstract:

Floating drug delivery systems (FDDS) are those systems which have a bulk density less than gastric fluids and because of these systems remains buoyant (3-4 hours) for a prolonged peroid of time in the stomach without affecting the gastric emptying rate. Based on the mechanisam of buoyancy, two distinctly different technologies have been utilized in the development of FDDS, which are effervescent system and non – effervescent system.

Keywords: *FDDS, buoyant , Gastric emptying rate, ,non – effervescent system.*

Corresponding author:

Chepuri .Madhavi

Associate Professor , Department of Pharmaceutics,
Sree dattha institute of pharmacy, Ibrahimpatnam, Telangana
E.mail:nellutla.jhancy@gmail.com

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INTRODUCTION:

FLOATING DRUG DELIVERY SYSTEMS (FDDS)

Floating drug delivery systems (FDDS) are those systems which have a bulk density less than gastric fluids and because of these systems remains buoyant (3-4 hours) for a prolonged period of time in the stomach without affecting the gastric emptying rate.

Based on the mechanism of buoyancy, two distinctly different technologies have been utilized in the development of FDDS, which are effervescent system and non – effervescent system.

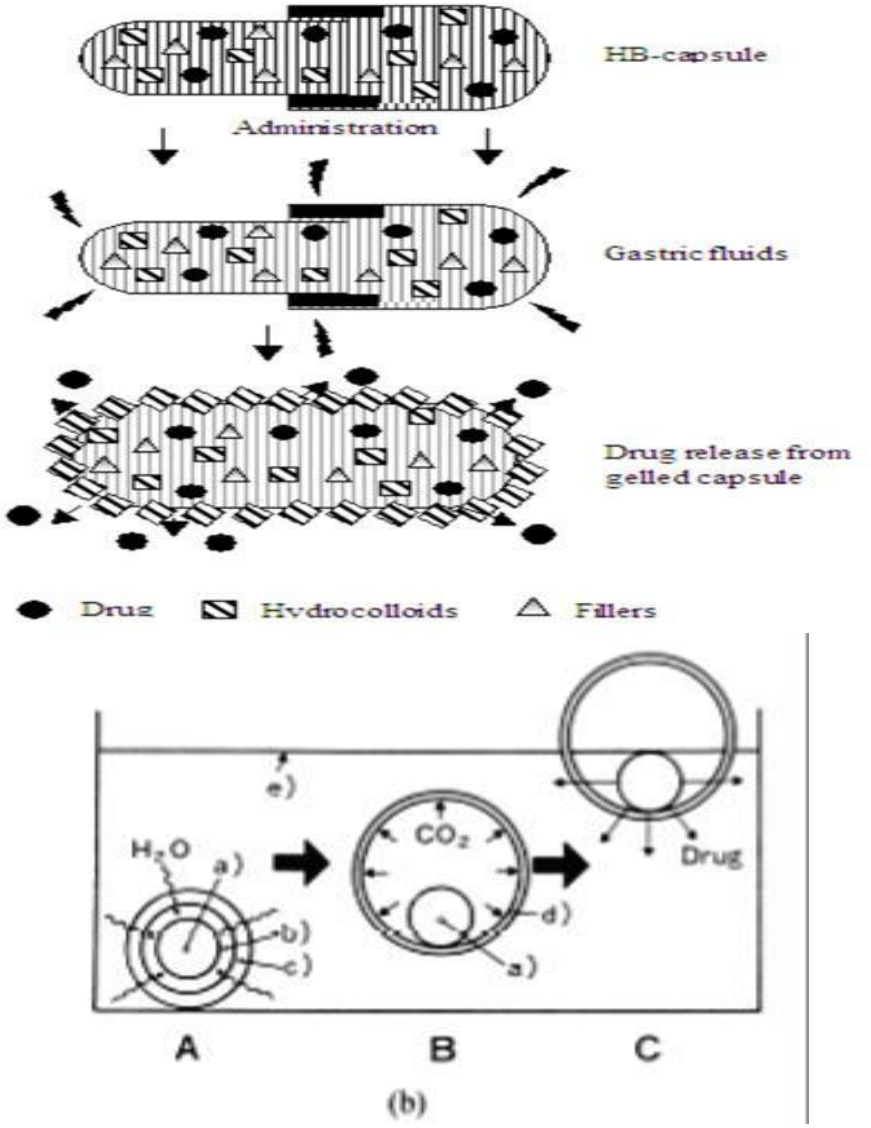
Effervescent system:

Effervescent systems include use of gas generating agents, carbonates (Sodium bicarbonate) and other organic acid (Citric acid and Tartaric acid) to produce carbon dioxide gas, thus reducing the density of the system and making it to float on the gastric fluid.

These effervescent systems further classified into two types

Gas generating systems

Intra gastric single layer floating tablet or Hydrodynamically balanced system.



A. Penetration of water
B. Generation of CO2 and floating
C. Dissolution of drug

Fig 1: Floating drug delivery systems (FDDS)

FORMULATION DESIGN

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Nimodipine (mg)	500	500	500	500	500	500	500	500	500
Sodium Alginate(mg)	250	500	750	250	500	750	250	500	750
Xanthan gum(mg)	250	500	750	-	-	-	-	-	-
Guar gum (mg)	-	-	-	250	500	750	-	-	-
Karaya gum(mg)	-	-	-	-	-	-	250	500	750
CaCO3(mg)	50	50	50	50	50	50	50	50	50
Calcium chloride(gm)	1	1	1	1	1	1	1	1	1

Preparation of Hydro gel beads of Nimodipine:
Method used – Ionotropic gelation method
Accurate quantity of polymer was dissolved in 50ml of distilled water and stirred to form dispersion. Drug was added to the above dispersion and again stirred for uniform distribution. and stirred until a homogenous mixture was obtained. The mixture was extruded through a 23G syringe needle into calcium chloride solution (1% w/v). The beads were allowed to remain in the same solution for 30 min to improve their mechanical strength. The formed beads were separated, washed with water and allowed to dry at room temperature overnight.

EVALUATION OF NIMODIPINE HYDROGEL BEADS:

Drug polymer interaction (FTIR) study:
Drug polymer interactions were studied by FT-IR spectroscopy. 100 mg of Nimodipine alone, mixture of drug and polymer, were weighed and mixed properly with potassium bromide uniformly. A small quantity of the powder was compressed into a thin semitransparent pellet by applying pressure. The IR-spectrum of the pellet from 500–4000 cm-1 was recorded taking air as the reference and compared to study any interference

Percentage yield:
Percentage practical yield of Nimodipine hydrogel beads was calculated to know about percentage yield or efficiency of any method, thus it helps in selection of appropriate method of production. Practical yield was calculated as the weight of Nimodipine beads recovered from each batch in relation to the sum of starting material.
The percentage yield of Nimodipine beads prepared was determined by using the formula.

$$\text{Percentage yield} = \frac{\text{Practical yield}}{\text{Theoretical yield}} \times 100$$

Surface morphology (SEM):
Scanning electron microscopy has been used to determine particle size distribution, surface topography, texture, and to examine the morphology of fractured or sectioned surface. SEM is probably the most commonly used method for characterizing drug delivery systems, owing in large to simplicity of sample preparation and ease of operation. SEM studies were carried out by using JEOL JSM T-330A scanning microscope (Japan). Dry Nimodipine gel beads were placed on an electron microscope brass stub and coated with in an ion sputter. Picture of Nimodipine hydrogel beads were taken by random scanning of the stub.

Buoyancy Behaviour:
The time between the introduction of the FDDS into the medium and its buoyancy to the upper one third of the dissolution vessel (floating lag time) and the time for which the formulation constantly floated on the surface of the medium (floating duration) were measured simultaneously as a part of dissolution studies.

Swelling Properties:
Swelling ratio was determined from the following equation:
Swelling ratio =
weight of swollen beads – initial weight of beads
initial weight of beads.

Drug Content:
The experiment was carried out in triplicate and drug loading was calculated from the following equation
Drug loading = Weight of drug in beads - Total weight of beads X 100

Drug Entrapment Efficiency:
The drug entrapment efficiency of prepared beads was determined by using the following equation.
EE (%) = Actual Drug Content / Theoretical Drug Content X 100

***In-vitro* dissolution studies**:
Procedure for In-vitro dissolution study:
The dissolution test was performed using 900 ml 0.1N HCL, in 37 ±0.5°C at 50 rpm. Nimodipine hydrogel beads equivalent to 30 mg of Nimodipine was used for the study. At various time points (hourly) 5ml of the sample solution was withdrawn from the dissolution apparatus for upto 12 hrs, and the samples were replaced with fresh dissolution medium. The samples were filtered and the absorbance was determined at 238nm.

Kinetics of drug release:
To examine the drug release kinetics and mechanism, the cumulative release data were fitted to models representing zero order (Q v/s t), first order [Log(Q0-Q) v/s t], Higuchi's square root of time (Q v/s t1/2) and Korsemeyer Peppas double log plot (log Q v/s log t) respectively, where Q is the cumulative percentage of drug released at time t and (Q0-Q) is the cumulative percentage of drug remaining after time t.

PREFORMULATION STUDIES:

Solubility study:
Nimodipine was found to be soluble in methanol, water, 0.1N HCL.
The solubility of Nimodipine in 10 mg/10 ml of solvent was carried out and the results revealed that Nimodipine was soluble in methanol and 0.1N HCL.

Melting point determination:
The melting point of Nimodipine was found to be 125° C.
The melting point of Nimodipine was found to be in range of 125° C.

Determination of λmax:
Wavelength of maximum absorption of Nimodipine in methanol solution of Nimodipine containing the conc. 10 µg/ ml was prepared in 0.1 N HCL and UV spectrum was taken using PG Instruments T60 double beam spectrophotometer. The solution was scanned in the range of 200 – 400nm. The maximum absorbance was found to be at 238nm.

Calibration curve of Nimodipine in 0.1NHCL.
10mg of Nimodipine was accurately weighed and transferred into 10ml volumetric flask. It was dissolved and diluted to volume with methanol to give stock solution containing 1000µg/ml. The standard stock solution was then serially diluted with methanol to get 1 to 10µg/ml . The absorbance of the solution was measured against methanol as blank at 238nm using UV spectrophotometer. The absorbance values were plotted against concentration (µg/ml) to obtain the standard calibration curve.

Calibration curve of Nimodipine at λmax of 238nm:
Standard calibration data of Nimodipine in 0.1N HCL

Table 1: Calibration curve of Nimodipine at λmax of 238nm

S.NO	**Concentration (µg/ml)**	**Absorbance (nm)**
1	0	0
2	2	**0.098**
3	4	**0.186**
4	6	**0.291**
5	8	**0.378**
6	10	**0.469**
7	12	**0.559**

Standard calibration curve of Nimodipine in 0.1N HCL

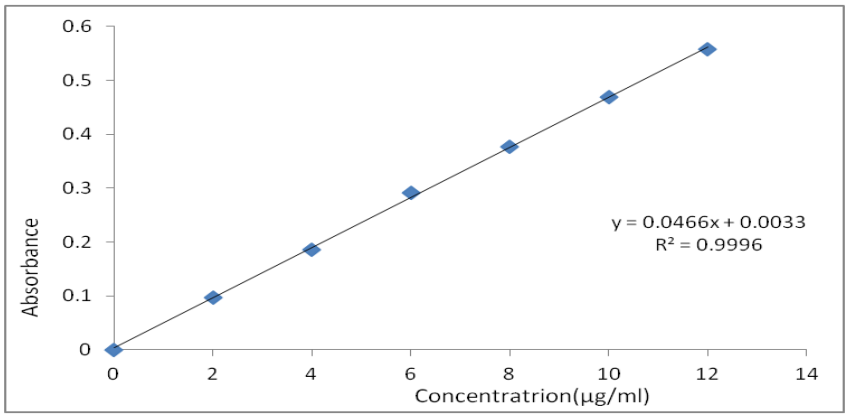


Fig 2: Standard calibration curve of Nimodipine in 0.1N HCL

EVALUATION OF NIMODIPINE HYDROGEL BEADS:

Drug polymer interaction (FTIR) study:

From the spectra of Nimodipine, optimized mixture of Nimodipine and polymer, it was observed that all characteristic peaks of Nimodipine were present in the optimized mixture, thus indicating that no interactions between drug and polymers used in the study.

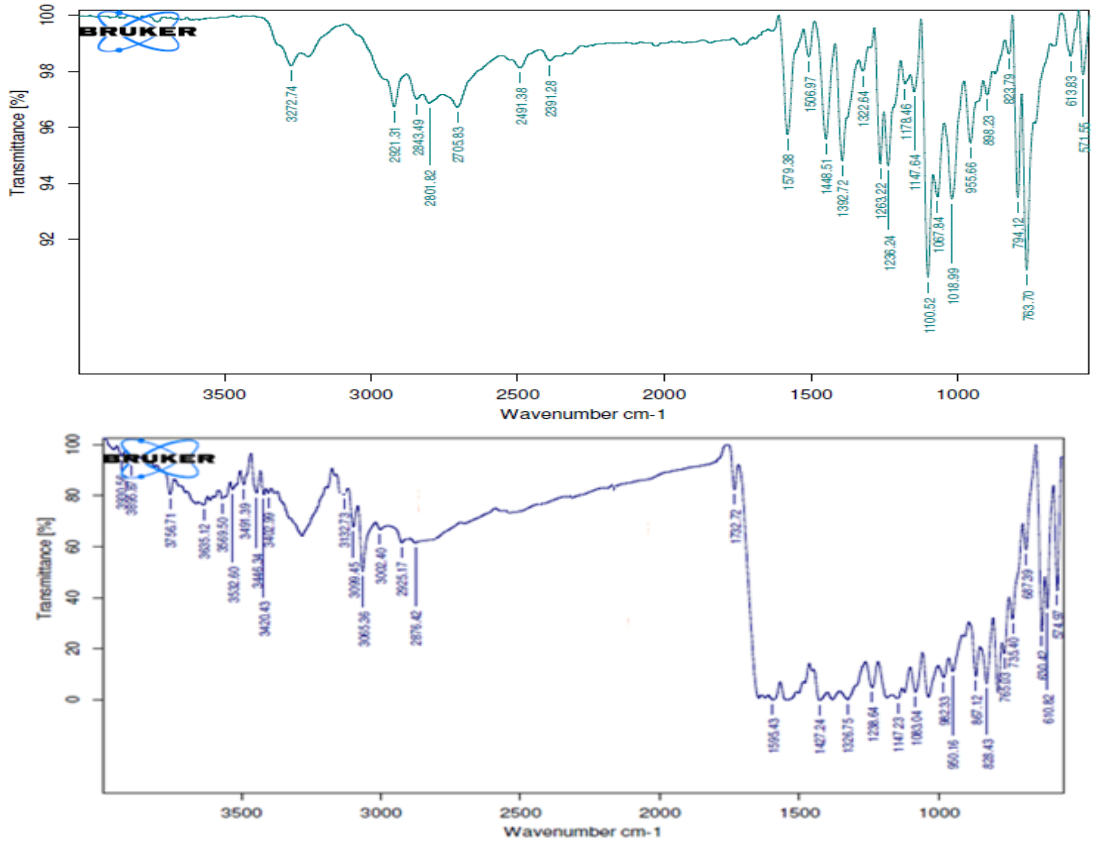


Fig 3: IR spectra of optimized formulation

Surface morphology - Scanning Electron Microscopy (SEM):

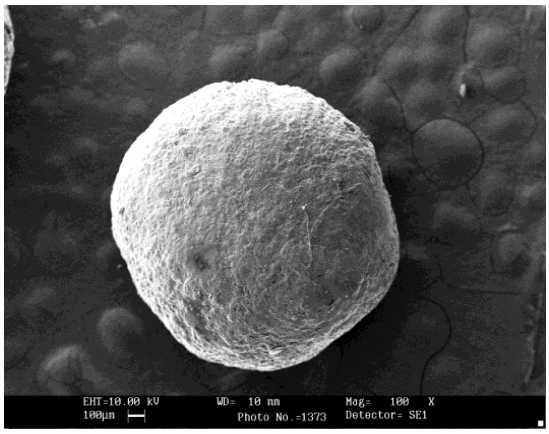


Fig 4: SEM photographs of Hydro gel beads using sodium alginate and karaya gum

The surface morphology of the Nimodipine beads was studied by SEM. Surface smoothness was observed with xanthan gum incorporated Nimodipine beads.

Determination of Average particle size:

Table 2: Average diameter of Nimodipine Hydro gel beads.

S.NO	**Formulation code**	**Average size (mm)**
1	F1	1.2
2	F2	1.3
3	F3	1.2
4	F4	1.4
5	F5	1.5
6	F6	1.2
7	F7	1.5
8	F8	1.3
9	F9	1.2

Buoyancy characteristics:

Table 3: Buoyancy characteristics of Nimodipine Hydrogel beads

S.NO	**FORMULATION CODE**	**FLT(SECS)**	**FLOATING DURATION(HRS)**
1	F1	88	6
2	F2	74	10
3	F3	52	12
4	F4	93	8
5	F5	76	10
6	F6	59	11
7	F7	97	8
8	F8	84	10
9	F9	63	11

The floating ability of prepared beads were evaluated. The beads remained a float throughout the study period (8-12hrs). It was observed that varying the polymer concentrations in the bead formulations did not affect the floating lag time or the floating duration of the beads in the dissolution media.

Table 4: Drug entrapment efficiency of Nimodipine Hydrogel beads

S.NO	FORMULATION CODE	PERCENTAGE YIELD	DRUG CONTENT (%)	ENTRAPMENT EFFICIENCY (%)
1	F1	**72.29**	**64.09**	**69.79**
2	F2	**84.63**	**80.36**	**83.71**
3	F3	**90.84**	**96.15**	**91.34**
4	F4	**66.26**	**68.27**	**70.82**
5	F5	**75.66**	**76.58**	**77.88**
6	F6	**89.92**	**82.19**	**86.93**
7	F7	**80.13**	**64.86**	**72.59**
8	F8	**84.02**	**79.09**	**85.46**
9	F9	**88.12**	**84.58**	**90.58**

***In vitro* dissolution studies:**

The results of the *in vitro* dissolution studies showed controlled release in a predictable manner. As the polymer concentration was increased, the drug release from the floating beads were found to decrease. Compared to guar gum karaya gum, xanthan gum retarded drug release more effectively, hydrogel beads had an optimum release at the end of 12th hour. The *in vitro* release profiles of all the formulations (F1 to F9).

***In vitro* dissolution studies:**

Table 5: *In vitro* release data of Hydrogel beads of Nimodipine

TIME(HRS)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
1	**29.52**	**22.59**	**9.68**	**37.64**	**26.28**	**19.54**	**28.65**	**36.15**	**27.62**
2	**40.29**	**36.15**	**16.56**	**50.48**	**37.83**	**28.19**	**36.21**	**44.29**	**39.42**
3	**58.65**	**44.29**	**29.32**	**67.34**	**45.06**	**37.54**	**58.28**	**56.42**	**46.09**
4	**66.21**	**56.42**	**36.18**	**75.15**	**58.03**	**45.15**	**64.25**	**63.21**	**58.48**
5	**78.28**	**63.21**	**49.42**	**82.42**	**66.46**	**55.07**	**79.94**	**71.41**	**65.21**
6	**84.25**	**71.41**	**56.02**	**90.26**	**73.9**	**64.47**	**86.61**	**79.24**	**73.02**
7	**90.94**	**79.24**	**67.48**	**93.34**	**81.94**	**76.35**	**99.29**	**85.54**	**81.24**
8	**93.61**	**85.54**	**79.36**	**97.62**	**94.18**	**85.66**		**92.62**	**89.62**
9	**99.29**	**91.62**	**86.10**		**98.66**	**90.54**		**99.58**	**90.56**
10		**96.58**	**92.22**			**94.02**			**95.21**
11		**99.02**	**94.52**			**99.88**			**98.26**
12			**97.26**						

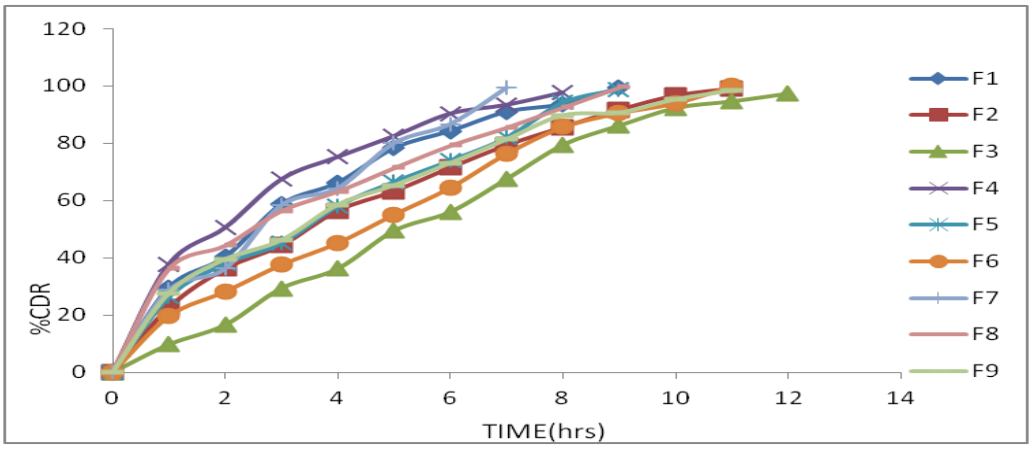


Fig :%CDR of F1-F9

Fig 5: *In vitro* dissolution studies

ZERO ORDER:

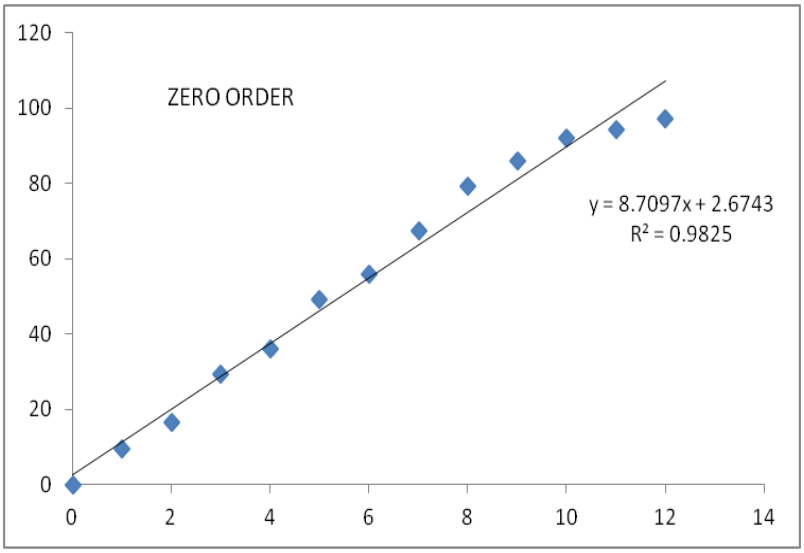


Fig 6: Release kinetics of Nimodipine hydrogel beads

Release kinetics of Nimodipine hydrogel beads:

The invitro dissolution data for best formulation F3 were fitted in different kinetic models i.e, zero order, first order, Higuchi and korsemeyer - peppas equation. Optimized formulation F3 shows R^2 value 0.982. As its value nearer to the '1' it is conformed as it follows the zero order release. The mechanism of drug release is further confirmed by the korsmeyer and peppas plot.

The 'n' value is 1.379 for the optimised formulation(F3) i.e., n value was >0.89 this indicates Super case II transport.

CONCLUSION:

- Preformulation studies like melting point, solubility and UV analysis complied with standards.
- The FT-IR Spectra revealed that, there was no interaction between Nimodipine and polymers.
- Surface smoothness of the Nimodipine beads was confirmed by SEM.
- As the ratio of polymer was increased, the mean particle size of Nimodipine floating beads was decreased. Nimodipine floating beads with normal frequency distribution were obtained.
- Entrapment efficiency increased with increase in the polymer concentration. From the results it can be inferred that there was a proper distribution of Nimodipine in the beads and the deviation was within the acceptable limits.
- The study also indicated that the amount of drug release decreases with an increase in the polymer concentration. The *in vitro* performance

of Nimodipine Hydrogel beads showed prolonged and controlled release of drug.

REFERENCES:

1. Yeole PG, Khan S, Patel VF. Floating drug delivery systems: Need and development. Indian J pharma Sci 2005;67(3):265-72.
2. Timmermans J, Moes AJ. Floating dosages forms: A Review. Int J Pharm1990;62:207-16.
3. Patel MG, Patel RH, Patel M, Patel KJ. Floating drug delivery system: An innovative approach to prolong gastric retention. Available at www.pharmainfo.net.aug.2010.
4. Srivastava AK, Narayanarao D. Floating microspheres of Cimetidine: formulation, characterization and in- vitro evaluation. Acta Pharm 2005;55:277-85.
5. Fursule RA, Patra CN, patil GB, Kosalge SB, patil PO, Deshmukh PK. Study of multiparticulate floating drug delivery system prepared by emulsion gelation technique. Int J Chem Tech Res 2009;1(2):162-7.
6. Jain AK, Jain CP, Tanwar YS, Naruka, PS. Formulation characterization and in vitro evaluation of floating microspheres of Famotidine as a gastro retentive dosage form. Asian J Pharm 2009;3(3):222-6
7. Sanjay K. Jain.,Design and Development of Hydrogel Beads for Targeted Drug Delivery to the Colon, satranidazole. AAPS PharmSciTech 2007; 8 (3)
8. Adhiyaman Rajendran.et.al.,Alginate-Chitosan Particulate System for Sustained Release of Nimodipine, Tropical Journal of Pharmaceutical Research, October 2009; 8 (5): 433-440
9. K.M. Manjanna.et.al.,Formulation and Optimization of Natural Polysaccharide Hydrogel Microbeads of Aceclofenac Sodium for Oral Controlled Drug Delivery, American Journal of Medical Sciences and Medicine, 2013, Vol. 1, No. 1, 5-17.
10. BHATT M. B.et.al.,Formulation And Evaluation Of Ionotropically Gelled Novel Hydrogel Beads Of Valsartan, IJPRBS, 2014; Volume 3(2): 845-859.
11. Payal Deepak.et.al.,Pioglitazone Loaded Chitosan Hydrogel Beads: Fabrication And In-Vitro Characterization, International Journal Of Pharma Professional's Research Volume-7, Issue-1, January-2016.